510K Summary

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K120169

AUG 24 2012

B. Purpose for Submission:

New device

C. Measurand:

Monoclonal Immunoglobulins (IgG, IgA, IgM) and light chains (kappa, lambda) in serum and urine

D. Type of Test:

Immunofixation Electrophoresis, Qualitative

E. Applicant:

Grifols Inc.

F. Proprietary and Established Names:

Immunofixation Electrophoresis Test using Interlab G26 Instrument

G. Regulatory Information:

1. Regulation section:
   21 CFR §866.5510 Immunoglobulins (A, G, M, D, E) Immunological Test Systems
   21 CFR §866.5550 Immunoglobulin (light chain specific) Immunological Test Systems
   21 CFR §862.1630 Electrophoretic, Protein Fractionation
2. Classification:
   Class II
3. Product code:
   CFF – Immunoelectrophoretic, Immunoglobulins (G, A, M)
   DFH – Kappa, Antigen, Antiserum, Control
   DEH – Lambda, Antigen, Antiserum, Control
   CEF – Electrophoretic, Protein Fractionation
4. Panel:
   Immunology (82)
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use:
   The Immunofixation Electrophoresis (IFE) Test using the Interlab G26 instrument is for the qualitative *in vitro* diagnostic separation and identification of abnormal immunoglobulins (IgG, IgA and IgM), and kappa and lambda light chains in human serum and concentrated urine using agarose gel supported on Mylar®. The test is useful as an aid in identifying suspected monoclonal proteins. The test result will be used in conjunction with clinical and other laboratory findings.

   The Interlab IFE kits, (2, 4, 6 samples per gel) are intended to be used with the automated Interlab G26 electrophoresis analyzer in conjunction with the Easy Mask antisera application device.
2. Indication(s) for use:
   Same as Intended Use.
3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:
Automated Interlab G26 ver. 2 electrophoresis analyzer in conjunction with the Easy Mask antisera application device and Elfolab software system version 16.1.0. (This Elfolab software system version 16.1.0 is an upgrade of version 7.3.0 previously cleared with Interlab Microgel Electrophoresis system cleared under 510(k) number k053571).

I. Device Description:

The Immunofixation Electrophoresis (IFE) Test kit is packaged as a 20 (2 samples/ gel), 40 (4 samples/ gel) or 60 (6 samples/ gel) test kits. The kit contains ready-to-use components: 10 gel plates, 2 buffered sponges, acid violet stain (500 mL), washing solution for applicators (80 mL), washing solution 1 for IFE (80 mL), washing solution 2 for IFE (80 mL), IFE diluent (6 or 12 mL), disposable sample trays 26 (10 pcs) or 39 (10 pcs), blotters A (10 pcs), blotters L (10 pcs), blotters G (10 pcs), and 1 CD Package Insert.

The following components are required for the test but are not supplied in the test kit: de-stain solution pack (6x100 mL), fixative solution (1.5 mL) and specific antisera Anti-Human-IgG (1 mL), Anti-Human-IgA (1 mL)), Anti-Human-IgM (1 mL), Anti-Human-Kappa (1 mL) and Anti-Human-Lambda (1 mL).

The Automated Interlab G 26 ver. 2 Electrophoresis Analyzer provides automated pipetting of samples from barcode sample tubes in a rack and dilutes the samples into a sample tray for dispensing onto an agarose gel. The protein fraction separation uses the principle of electrophoresis; separation involving electrically charged molecules that orient and migrate at different rates when subjected to an electric field. The migration is performed at a constant temperature, obtained through the use of a Peltier device, on assay specific buffered agarose gel plates. The agarose gel medium provides a support and molecular sieve allowing the different fractions to migrate to points based on individual net charges.

After electrophoresis, the gel is heated to "fix" the focalized proteins, followed by assay specific staining, destaining, washing and drying. All methods utilizing a quantitative assessment are immediately processed using the on-board densitometer. The signal obtained for each specimen result is sent to the personal computer and presented using the Elfolab interpretive software. The Interlab G26 instrument is pre-programmed with all necessary firmware to conduct and manage all phases of the analytical procedures used in Interlab manufactured assays. The instrument works in conjunction with a personal computer using Windows® based software featuring pull down menus and intuitive icons for easy instrument control, selection of analytical methods, and data evaluation.

Instrument design includes: automated application of the samples on the agarose gel; electrophoretic migration; "heat fixing" proteins to the gel; gel staining/ destaining/ drying; densitometric reading of the gel; and data transmission and processing.

The Interlab Easy Mask Antisera Applicator Device is a standalone electronic instrument identical to the peltier contained within the Interlab G26 and is designed to work in conjunction with the Interlab G26. This device allows for accurate and simplified processing of various electrophoretic agarose gel assays that require reagent or antisera overlays. This device allows for easier user processing of the

manual steps necessary in antisera type assays (IFE, BJ, Penta) by allowing the user to work unencumbered from mechanical arms and instrument covers.

The Easy Mask provides functions identically to the processing steps used in other agarose gel systems that require the user to perform the manual antisera steps directly on the instrument. Through the use of a Peltier and vacuum pump, the temperature across the surface of the gel remains at a precise and controlled temperature, thus improving assay quality and decreasing processing time. Instrument is designed to receive the Gel Holder from the Interlab G26 Instrument. The Gel Holder is inserted into a template which places the gel in direct contact with the peltier plate assuring uniform and controlled temperature over the entire surface of the gel. Perfect adhesion of the gel to the peltier plate is accomplished using a vacuum pump. Assay specific application masks are placed in the frame, which provide precise application of the antisera or reagents during the incubation phase. After the incubation phase is complete, the frame locks over the gel providing a calibrated heated press to blot away un-bound antisera and reagents. When processing is completed on the Easy Mask, the operator places the Gel Holder back in the parking location on the Interlab G26 for the final steps of the analysis.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) number(s):
   Immunofixation Electrophoresis Test using Interlab G26 Instrument (k103757)

2. Comparison with predicate:

	Predicate G26 ver.1	G26 ver. 2
Instrument	Automated Interlab G26 electrophoresis analyzer. Instrumentation includes the Easy Mask antisera application device and the Elfolab software system.	Automated Interlab G26 electrophoresis analyzer. Instrumentation includes the Easy Mask antisera application device and the Elfolab software system.
Methodology	Gel Electrophoresis	Same
Technology	Agarose gel Electrophoretic Migration with Immunofixation	Same
Sample type	Serum and urine	Same
Sample size	30 µL	Same
Results Interpretation	Qualitative	Same
Automated Application of Samples on the Agarose Gel	Yes	Yes
Heat Fixing Proteins to Gel	Yes	Yes
Gel Staining	Yes	Yes
Gel Destaining	Yes	Yes
Gel Drying	Yes	Yes
Densitometric Reading of the Gel	Yes	Yes

Data Transmission and Processing	Yes	Yes
Positive patient ID from Tube Barcode	No, Manual by Tech	Yes
Primary Tube Sampling	No, Manual by Tech	Yes
Sample Dilutions	No, Manual by Tech	Yes
Lowest Detectable Limit	Serum: IgGλ: 0.05 g/L IgAκ: 0.03 g/L IgMλ: 0.06 g/L Urine: IgGκ: 0.028 g/L IgAλ: 0.050 g/L IgMκ: 0.062 g/L	Serum: IgGκ: 0.05 g/L IgAλ: 0.03 g/L IgMκ: 0.06 g/L Urine: IgGκ: 0.028 g/L IgAλ: 0.050 g/L IgMκ: 0.062 g/L

K. Standard/Guidance Document Referenced (if applicable):
CLSI EP-7A: Interference Testing in Clinical Chemistry

L. Test Principle:
The principle of Immunofixation electrophoresis (IFE) is based on the protein separation at alkaline pH. After protein migration, one of the gel lanes is treated with fixative to fix all proteins to provide a reference pattern and the other gel lanes are treated with specific antisera. Reaction with patient samples results in the formation of insoluble antigen-antibody complex that produces a band of precipitate when the proportion of antibodies and antigen is appropriate. The precipitation rate depends on temperature, pH, and ionic strength of the solution. The gels are washed to remove excess un-precipitated proteins, then blotters are applied to remove excess buffer twice. Gels are then stained with acid violet, de-stained and dried.
The comparison of the positions of immunofixed bands and that of the suspected monoclonal band in the reference pattern allows assessment of the biochemical identity of the protein. IFE usually displays discrete and sharply focused bands with monoclonal proteins in monoclonal gammopathies. In polyclonal gammopathies a diffuse zone is shown in the corresponding antiserum in contrast to the sharp band observed in monoclonal gammopathies.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:
   Within-Run Reproducibility: Two series of eight samples were analyzed. For each series, one normal serum and seven sera with confirmed monoclonal bands representing all subtype were run. For series 1 were run (IgG κ. IgG λ, IgA κ, IgA λ, IgM κ, IgM λ, κ free), and (IgG κ. IgG λ, IgA κ, IgA λ, IgM κ, IgM λ, λ free) for series 2. For each sample, six replicates were run on the agarose gel plates, using the same batch of reagents. Results were evaluated by visual inspection.

   The Within-run precision study showed 100% agreement and reproducibility.
   Between-Run Reproducibility: Study was performed to evaluate the reproducibility in

different runs of the same batch of reagents, four cycles of three agarose gel plates were used to analyze replicates of eighteen samples (three normal sera and fifteen sera with confirmed monoclonal bands) representing all the subtype (IgG κ. IgG λ, IgA κ, IgA λ, IgM κ, IgM λ, λ free, κ free). Patterns obtained on the agarose gels were evaluated by visual inspection. Inter-run Precision Study showed 100% concordance and reproducibility.
The Between-run precision study showed 100% agreement and reproducibility.

Inter-Lot Reproducibility: Study was performed to evaluate the activity of different batches of antisera. For this study, three different batches of antisera were used to analyze a series of nine agarose gel plates. Nine different samples were analyzed, one normal serum and eight sera with confirmed monoclonal bands, one sample for each subtype (IgG κ. IgG λ, IgA κ, IgA λ, IgM κ, IgM λ, λ free, κ free). Patterns were evaluated by visual inspection. Since this method is based only on a qualitative analysis, the precision was evaluated only on results accordance. The inter-lot precision study showed 100% agreement and reproducibility.

b. *Linearity/assay reportable range:*
Not applicable.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):* No reference standards and method available.

Stability: Real time stability studies were performed on four packs of IFE Kit and four packs of antisera kit on IgG., IgGλ, IgAκ, IgAλ, IgMκ, and IgMλ samples. Kits were stored at room temperature and tested every 6, 12, 18, and 24 months. The studies support the antisera stability for 24 months. Open kit and open antisera vial studies were performed on four packs of IFE Kit and four packs of antisera kit. IFE kits were stored at room temperature (15-30°C) and antisera kits were stored at 2 – 8°C. Both open IFE kits and antisera kits were tested at 6 months. The studies support the open kit and open vial stability for 6 months.

d. *Detection limit:*
Serial dilutions will be prepared from three (3) pathological serum samples containing the different types of the confirmed monoclonal bands (IgG k, IgA λ, and IgM K) as shown in table A. We compared the dilution made manually and run on the G26v1 and the dilution made from the dilutor on the G26v2 (with auto sampler on board.)
For each type of the monoclonal band (IgG k, IgA λ, and IgM K), the lowest band concentration for the monoclonal component will be examined by visual inspection individually and further determined to be the detection limit.

Monoclonal Component	**Concentration Band (g/L)**	**Detection Limit (g/L)**
IgG- Kappa	20.5	0.05
IgA- Lambda	22.5	0.03
IgM- Kappa	12.8	0.06

e. Analytical specificity:

Interference:

An interference study was performed to evaluate if potentially interfering substances such as bilirubin, hemoglobin and lipids show interference effect with serum samples with the Interlab IFE test showed 100% agreement between spiked and un-spiked samples identifying equivalent band patterns. No missed or additional bands were observed. No bands were detected in the normal sample. No interference was observed from bilirubin (up to 20 mg/dL), hemoglobin (up to 500 mg/dL), and lipemia (up to 220 mg/dL) on the test.

Eight urine samples comprised of seven pathological bands representing a mix of all subtypes and one normal, were run on the Interlab G26 instrument. The Interlab IFE test showed 100% agreement between spiked and un-spiked samples identifying equivalent band patterns. No missed or additional bands were observed. No bands were observed in the normal patients. Samples show no interference effect from Hemoglobin (up to 500 mg/dL).

Applicator Carryover:

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Serum

A Comparison study was performed to compare the device G26 v2 (with auto-sampler) with the FDA cleared predicate device (k103757), Interlab G26 v1 (without auto-sampler) . We performed the comparison using our FDA cleared (k103757) kits for the IFE immunofixation test; SRE627K (2 sample), SRE628K(4 sample) and SRE643K(6 sample).

The monoclonal bands from the results of the immunofixation electrophoresis kits were evaluated by visual inspection. If the monoclonal banding patterns from the new device (G26 v2) and the predicate are qualitatively identical, the result is concordant; otherwise, it is discrepant.

On both G26 v1 and v2 (with auto-sampler), a series of 102 serum samples obtained from normal (10 samples) and suspected pathological (92 samples) patients containing monoclonal and polyclonal proteins were tested using the Interlab IFE Acid Violet electrophoresis test system. The samples contained a mixture of different subtypes (IgG κ. IgG λ, IgA κ, IgA λ, IgM κ, IgM λ, λ free, IgG λ & IgA λ, IgG λ & IgM λ, IgG k & IgM λ, IgG λ & λ free, IgM k & IgM λ, IgG k & IgG k).

The Interlab IFE test showed 100% agreement to the reference method in identifying equivalent band patterns. No missed or additional bands were observed in either method. Neither method detected bands in the normal patients. No false bands were identified.

Number of samples	Concentration	Subtype	Total Serum Protein (g/dL)
41	< 0.8 g/dl	IgM K/L, IgA k/ L, IgG K/L	8 - 9.5
34	0.8 – 2 g/dl	IgM K/L, IgA k/ L, IgG K/L	10 - 10.9
21	>2 g/dl	IgM K/L, IgA k/ L, IgG K/L	11 - 13
3	>20 mg/L	λ free	11
10	n.a.	Negative	9
Total 109			

Urine

A Comparison study was performed to compare the device G26 v2 (with auto-sampler) with the FDA cleared predicate device (k103757), Interlab G26 v1 (without auto-sampler) . We performed the comparison using our FDA cleared (k103757) kits for the IFE immunofixation test, SRE627K (2 sample), SRE628K(4 sample) and SRE643K(6 sample).

The monoclonal bands from the results of the immunofixation electrophoresis kits were evaluated by visual inspection. If the monoclonal banding patterns from the new device (G26 v2) and the predicate are qualitatively identical, the result is concordant; otherwise, it is discrepant.

A mix of urine samples were run on the Interlab G26 version 1 and G26 version 2.

Samples were centrifuged at 5000 rpm for 5 min and then concentrated, if necessary, by using Millipore Minicon Concentrator in a range of 20X – 80 X. Sample were run following the manufacturer's instructions.

A total of 64 samples were run for the comparison study, the 64 samples were comprised of 56 pathologic samples and 8 Negative samples. The 64 samples were comprised of 6 samples with no detected values for total urine proteins in the 24h, 39 samples with < 2000 mg/24h of total proteins in the urine and 19 samples with >2000 mg/24h of total proteins in the urine.

The Interlab IFE test showed 100% agreement to the reference method in identifying equivalent band patterns. No missed or additional bands were observed in either method. Neither method detected bands in the normal patients. No false bands were identified.

Number of Samples	Concentration	Subtype	Total Urine Protein (mg/24 h)
39	>20 mg/L	K free and λ free	< 2000
19	>100 mg/L	Polyclonal	>2000
6	< 0.8 g/dL	IgG K	n.d
Total 64			

3. Clinical studies:

a. *Clinical Sensitivity:* Not applicable.

b. *Clinical specificity:* Not applicable.

c. *Other clinical supportive data (when a. and b. are not applicable):* Not applicable

4. Clinical cut-off:
   Same as Expected values/Reference range.

5. Expected values/Reference range:
   Absence of monoclonal immunoglobulins.

   References cited: '*Tietz Fundamentals of* Clinical Chemistry', Carl A. Burtis, Edward R. Ashwood, MD, page 346, Fifth Edition,(1996) and 'Primer of Immunoelectrophoresis with interpretation of Phathologic Human Serum Patterns', S. Karger, pp 6-29. Arcquembourg, P.C.; Salvaggio J.E.; Bicker J.N. (1970).

N. Instrument Name:

Automated Interlab G26 ver. 2 electrophoresis analyzer in conjunction with the Easy Mask antisera application device

O. System Descriptions:

1. Modes of Operation:
   Protein separation and detection of the separated proteins on Immunofixation gels (2, 4. or 6 samples per gel).
2. Software:
   The Interlab operating system Elfolab software version 16.1.0 is designed to work with the Interlab G26 instrumentation. FDA has reviewed and found the following software documents acceptable: Device Hazard Analysis, SRS, Architecture Design Chart, SDS, Traceability Analysis, Software development Environment Description, Summary of Verification and Validation Results, Revision Level of history, Unresolved anomalies (bugs and defect) and Operation Manual for the Serum and Urine IFE line of product types.
3. Specimen Identification:
   Bar code
4. Specimen Sampling and Handling:
   Automated pipettor
5. Calibration:
   Not applicable.
6. Quality Control:
   Not Applicable

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

None.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Grifols, Inc.
c/o Gary Lehnus
Lehnus & Associates Consulting
150 Cherry Lane Rd,
East Stroudsburg, PA 18301

AUG 24 2012

Re: k120169
Trade/Device Name: Interlab IFE test using G 26 v2.0 Instrument
Regulation Number: 21 CFR §866.5510
Regulation Name: Immunoglobulins IgG, IgA, IgM, Kappa and Lambda Immunological Test Systems
Regulatory Class: II
Product Codes: CFF, DFH, DEH, CEF
Dated: August 22, 2012
Received: August 23, 2012

Dear Mr. Lehnus:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter

will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Maria M. Chan

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K120169

Device Name: Immunofixation Electrophoresis Test using Interlab G 26 v2.0 Instrument

Indications For Use:

The Immunofixation Electrophoresis (IFE) Test using Interlab G 26 v2.0 instrument is for the qualitative in vitro diagnostic separation and identification of immunoglobulins (IgG, IgA and IgM), and kappa and lambda chains in human serum and concentrated urine using agarose gel supported on Mylar®. The test is useful as an aid in identifying suspected monoclonal proteins. The test result is to be used in conjunction with clinical and other laboratory findings.

The Interlab IFE kits 2, 4, and 6 samples per gel, are intended to be used with the automated Interlab G26 v1.0 and v2.0 electrophoresis analyzers in conjunction with the Easy Mask antisera application device.

Prescription Use X AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510K K120169